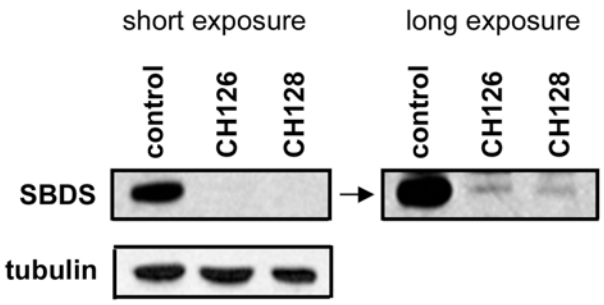
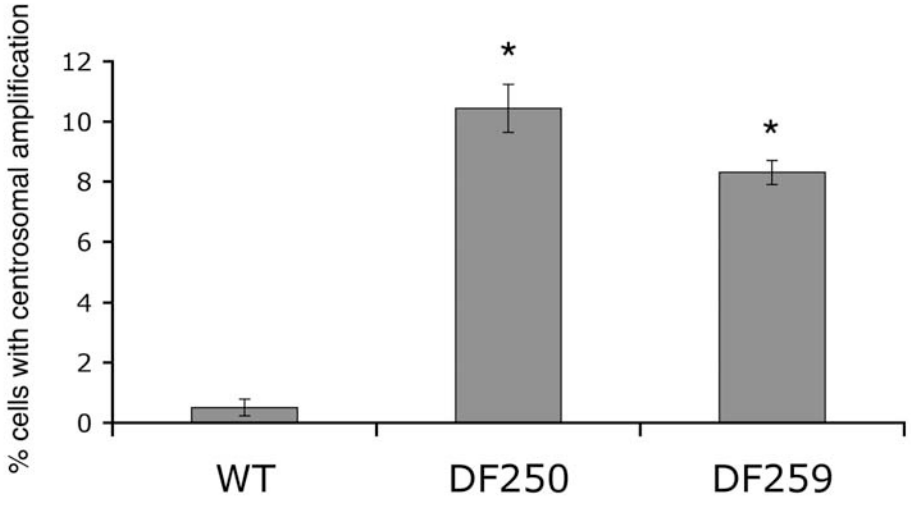
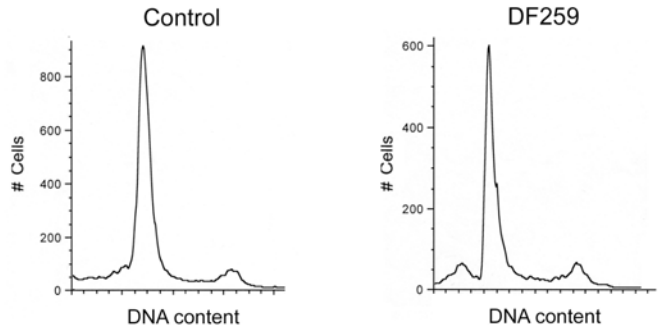
Supplementary Figure 1



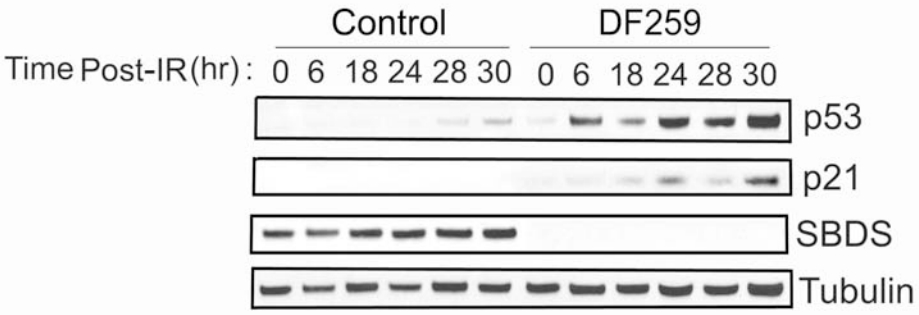
Supplementary Figure 2



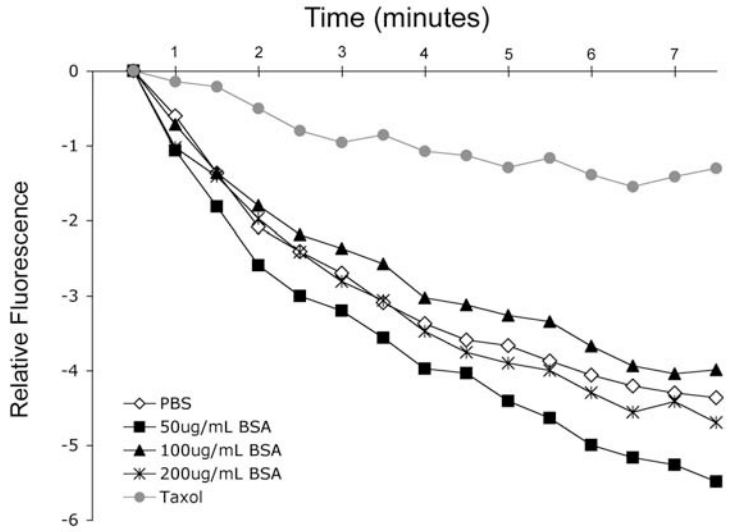
Supplementary Figure 3



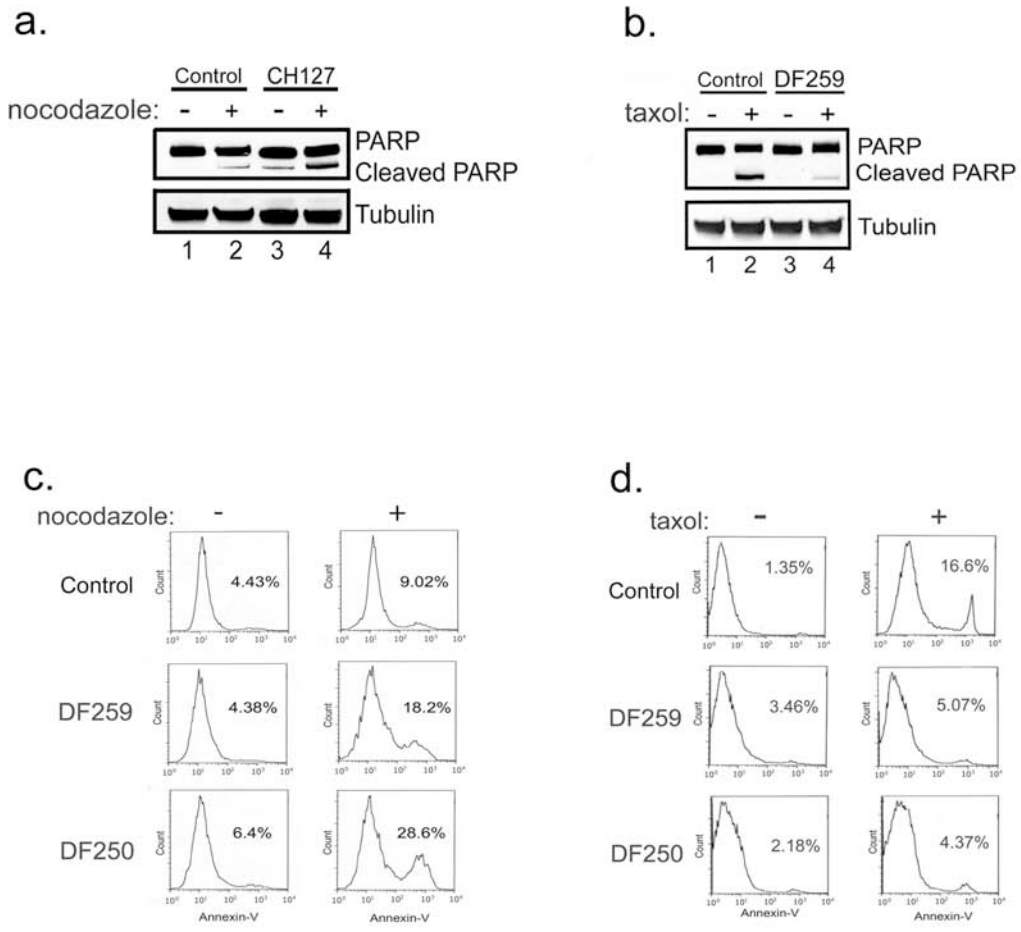
Supplementary Figure 4



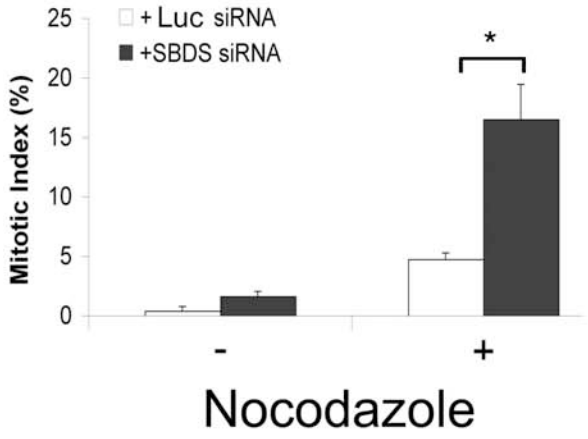
Supplementary Figure 5



Supplementary Figure 6



Supplementary Figure 7



Supplementary Figure Legends

Supplementary Figure 1: SBDS protein expression in SDS patient cells.

Primary BMSC lysates from a normal control or two SDS patients (CH126, CH128) were blotted for SBDS protein. Both long and short exposures of the western blot are shown. A scant amount of SBDS protein is visible in SDS patient lysates following a long exposure of the blot. Tubulin was blotted as an internal protein standard to confirm equal protein loading. Similar results were obtained with lysates from DF250, DF259, CH127, and DF1227.

Supplementary Figure 2: Centrosomal amplification in SDS patient-derived lymphoblasts.

EBV-immortalized lymphoblast cell lines from healthy controls or SDS patients were fixed and stained with antibodies against pericentrin and tubulin. Cells with three or more centrosomes were scored. *$p<0.01$.

Supplementary Figure 3: Apoptosis is increased in SDS patient cells.

EBV-immortalized lymphoblast cultures from a normal control or an SDS patient (DF259) were analyzed for DNA content by flow cytometry as described in the methods. A sub-G1 apoptotic cell population was increased in the DF259 cells compared with the normal control cells. Lymphoblasts from DF250 yielded similar results.

Supplementary Figure 4: The p53 DNA damage response is intact in SDS patient cells. Primary BMSC from an SDS patient (DF259) or a normal control were treated with 4Gy of γ–radiation. Cells were lysed at the indicated times (hours) post-irradiation and analyzed by immunoblot using the indicated antibodies.

Supplementary Figure 5: A BSA protein control does not affect microtubule stability.

Increasing concentrations of purified bovine serum albumen (BSA) as indicated were added to pre-formed microtubules and microtubule depolymerization was assessed as described in Fig 3c. BSA concentrations of 0.74uM, 1.5uM, and 3uM were assayed. No significant effect of BSA on microtubule depolymerization was noted in three independent experiments. A representative experiment is shown.

Supplementary Figure 6: Apoptosis in response to nocodazole and taxol.

a and b: Lymphoblast cell lines originating from SBDS-/- patients (CH127, DF259) or normal control lymphoblasts were treated with nocodazole (a) or Taxol (b). PARP cleavage was assessed by western blot. Tubulin was blotted to confirm equal protein loading.

c and d: Lymphoblasts from normal controls or SDS patients (DF259, DF250) were treated with nocodazole or taxol. Cells were fixed, stained for Annexin V and analyzed by flow cytometry. The percentage of Annexin V-positive apoptotic cells is indicated in (c) and (d). Two independent experiments were performed.

Supplementary Figure 7: SBDS siRNA knock-down promotes nocodazole-induced mitotic arrest.

Wild-type GM00038 skin fibroblasts were infected with lentivirus vectors encoding siRNA directed against SBDS or against Luciferase. Cells were treated with nocodazole and the mitotic index was calculated as described in (a). *$p<0.05$.

Supplementary Table 1: SBDS Genotypes

Patient ID#	SBDS mutations
DF250	IVS2+2 T>C IVS3-1 G>A
DF259	c183_184 TA>CT (chain termination (K>X) in exon 2 at codon 62) IVS2+2 T>C
DF1227	c183_184 TA>CT IVS2+2 T>C
CH126	c183_184 TA>CT IVS2+2 T>C
CH127	c183_184 TA to CT IVS2+2 T>C
CH128	c183_184 TA>CT IVS2+2 T>C